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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/928,614	08/13/2001	Heng Zhong	S-31514A	7523

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EXAMINER	
KALLIS, RUSSELL	
ART UNIT	PAPER NUMBER
1638	

DATE MAILED: 04/22/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/928,614	ZHONG ET AL.	
	Examiner	Art Unit	
	Russell Kallis	1638	

-- Th MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period f r Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 March 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disp sition of Claims

4)☒ Claim(s) *1-16 and 18-50* is/are pending in the application.

4a) Of the above claim(s) *14-16,25-28 and 30-50* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-13, 18-24, and 29* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Applicant's election without traverse of Group VI in Paper No. 9 is acknowledged.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-13, 18-24, and 29 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for *Agrobacterium tumefaciens*-mediated transformation of multiple shoot cultures of melon, watermelon, and squash from *Cucurbitaceae* and multiple shoot cultures of sugar beet and sunflower, said multiple shoot cultures generated from meristematic tissue-containing explants; does not reasonably provide enablement for multiple shoot cultures from *Chenopodia* or any other dicotyledonous genera, other *Agrobacterium* species, other means of transformation, or the use of non-meristematic tissue explants or callus for the formation of multiple shoot cultures. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

Applicant broadly claims a method of transforming and regenerating a dicotyledonous plant using any transformation method including either *Agrobacterium* infection or biolistic bombardment of multiple shoot cultures generated from meristematic tissue or callus on culture medium having cytokinin levels from 0.01 mg/L to 25 mg/L.

Applicant teaches a method for transformation of multiple shoot meristematic cultures of squash, watermelon, melon, and sunflower and regeneration of transformed plants thereof (Examples 1-4, pages 29-36) and transformation and regeneration of viable and fertile sugar beet plants expressing GUS in T1 seeds (Example 5, pages 36-41).

Applicant does not teach conditions for generating multiple shoot culture and conditions that promote shoot elongation in dicotyledonous plants other than in the families *Cucurbitaceae* and *Chenopodiaceae* (only beet is described), and in Sunflower, or a method for transformation of all dicotyledonous plants using any bacterium of the genus *Agrobacterium* or a method for generating multiple shoot cultures from non-meristematic tissue containing explants or callus.

Many dicot species continue to demonstrate recalcitrance to transformation. Attempts to transform various ecotypes of *Arabidopsis* have demonstrated that there are several different steps in the interaction between the plant and vector blocking transfer of the DNA common to all plants. One instance, that also shows recalcitrance to transformation, is apparently independent of plant-vector interactions. The integration of the foreign DNA into the host genome necessary for transformation by any method was not observed even though the DNA had made it into the nucleus. This suggests that not only the necessary co-evolved interactions between *Agrobacterium* and a plant may be absent in many plants that have no history of association with *Agrobacterium*, but there are also non-*Agrobacterium* associated abilities such as the ability to integrate foreign DNA that are unexpected in attempting to transform recalcitrant dicots (Gelvin S. *et al.,* The Plant Cell, March 1997, Vol. 9; pp. 317-333; page 317 column 1, line 13 to page 318 column 1, to the end of the introduction).

Further, the sensitivity of various ecotypes within a species known to be competent for *Agrobacterium* transformation is known to vary to such an extent that the possibility of either low frequency or no transformation events using *Agrobacterium* would require testing for successful transformation under a variety of phytohormone treatments. This is demonstrated in transformation of the genus *Populus* and woody perennial species in general using disarmed *Agrobacterium tumefaciens* by Han *et al.* (Can. J. For. Res. 27: 464-470, 1997) and in *Arabidopsis* genotypes by Chateau S. *et al.* (J. of Experimental Botany, December 2000; Vol. 51, No. 353; pp. 1961-1968). Specifically, Han notes a requirement for genotype specific culture conditions customized to promote cell competence for regeneration (page 464 column 2, lines 1-25) and Chateau remarks upon the frequently observed requirement for well-defined tissue culture conditions that were required to overcome the genotype effect often found in *Agrobacterium tumefaciens* mediated transformation methods (page 1962 column 1, lines 16-25).

The unpredictability inherent in adapting transformation methods with tissue culture method is shown in the number of multiple insertion events at the same locus in the genome of a transformed plant with a high degree of rearrangements of the transforming DNA in almost all the lines recovered (Kohli A. *et al.,* PNAS, June 1998, Vol. 95 ; pages 7203-7208 ; see 7205 column 2, lines 29-37and Table 1 page 7206). Although tDNA had been integrated, the extent that the formation of chimeric structure would result in a phenotype is unpredictable. Further, it is well known in the art that multiple insertion events give rise to gene silencing and often result in the reduction or elimination of expression of the desired gene, which is the exact opposite result of what was originally intended.

Furthermore, transformation methods are known to hinder the ability of known tissue culture methods to produce whole plants. It is well known in the art that direct DNA transfer transformation methods are inherently unpredictable and require rigorous testing (Potrykus I. *et al.,* Biotechnology 1990, pages 535-542; page 539 to 541, Examples 7-12, 14-17, and 19-21).

Moreover, shoot tip cultures are produced from meristematic cells and not non-meristematic callus (Claim 4). Callus generated from embryonic tissue is cultured in a callus phase. Upon transformation and selection organs are induced from the undifferentiated callus tissue. Shoot tip culture is derived from meristematic cells. (Hansen G. *et al.,* Trends in Plant Science June 1999, Vol. 4, No. 6, pages 226-231; page 226 column 2 line 14 to page 227 column 2 line10).

Considering the absence of guidance provided for transformation of all dicot species by any means including either *Agrobacterium* or biolistics as broadly set forth in the claims, and given the unpredictability in the art, undue trial and error experimentation would be required to screen through the multitude of non-exemplified combinations of explants types, media components and conditions for multiple shoot propagation, transformation, and regeneration of each and every non-exemplified dicot species, notably the *Curbitaceae* family and *Chenopodia* family, encompassed by the scope of the claims to find culturing conditions that would successfully transform and regenerate any dicot species transformed with disarmed *Agrobacterium tumefaciens* or other *Agrobacterium* species. Undue experimentation would have also been required to adapt biolistics or other transformation methods to shoot tip culture protocols for obtaining stably transformed plants.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-13, 18-24, and 29 are rejected under 35 U.S.C. 103(a) as being unpatentable over Tuli R. *et al.,* U.S. Patent 6,242,257 filed May 22, 1997 in view of Rangan T. *et al.* U.S. Patent 5,834,292 filed May 8, 1995 and Jefferson R. *et al.,* (EMBO Journal, 1987, Vol. 6, No. 13, pages 3901-3907).

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Applicant broadly claims a method of transforming a dicotyledonous plant with a GUS gene using either *Agrobacterium* infection or biolistic bombardment of multiple shoot cultures generated from meristematic tissue wherein the cytokinin in the culture medium is between about 0.01 mg/L to about 25 mg/L.

Tuli teaches a method of regenerating viable and fertile cotton plants by tissue culture manipulation of an apical meristem in culture medium having 0.1 mg/L to 100 mg/L cytokinin (columns 17-21).

Tuli does not teach *Agrobacterium* inoculation of a wide range of cotton explant types and transformation using the GUS marker gene.

Rangan teaches *Agrobacterium* inoculation of a wide range of cotton explant types (Examples 18-26 columns 25-27).

Jefferson teaches transformation using the GUS marker gene and its' advantages over other selectable markers (entire Abstract; page 3901 column2, bottom 2 paragraphs; page 3902 column 1, top paragraph).

It would have been obvious at the time of Applicant's invention to modify the invention of Tuli to include a polynucleotide encoding GUS taught by Jefferson and the method steps for *Agrobacterium* and transformation of cotton taught by Umbeck. One of ordinary skill in the art would have been motivated by the teachings of Tuli that multiple shoot culture technique is a useful for genetic engineering of a wide range of plants by *Agrobacterium* transformation (column 4 lines 16-33, column 9 lines 39-53, and column 13 lines 20-29), the teachings of *Agrobacterium* inoculation of a wide range of cotton explant types by Rangan, the teachings of the ease and wide applicability of the GUS marker by Jefferson, and that one would have had a reasonable expectation of success of expressing genes in transformed plants and plant cells.

All claims are rejected.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Russell Kallis whose telephone number is (703) 305-5417. The examiner can normally be reached on Monday-Friday 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson can be reached on (703) 306-3218. The fax phone numbers for the Group is (703) 308-4242 or (703) 305-3014.

Any inquiry of a general nature or relating to the status of this application or proceeding, or if the examiner cannot be reached as indicated above, should be directed to the receptionist, whose telephone number is (703) 308-0196.

Russell Kallis Ph.D.
April 14, 2003

DAVID T. FOX
PRIMARY EXAMINER
GROUP ~~180~~ 1638